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2011-12

Veritor™ System

For Rapid Detection of Flu A+B

CLIA-waived kit configured for testing nasal and nasopharyngeal swab samples freshly collected, processed and dispensed directly onto assay test device.

30
Determinations

BD Veritor™ System

For Rapid Detection of Flu A+B

CLIA Complexity-WAIVED

For use with nasal and nasopharyngeal swab specimens.

For *in vitro* use only.

A Certificate of Waiver is required to perform this test in a CLIA waived setting. To obtain a Certificate of Waiver, please contact your state health department. Additional CLIA waiver information is available at the Centers for Medicare and Medicaid website at www.cms.hhs.gov/CLIA or from your state health department.

Failure to follow the instructions or modification to the test system instructions will result in the test no longer meeting the requirements for waived classification.

INTENDED USE

The **BD Veritor™** System for Rapid Detection of Flu A+B is a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasal and nasopharyngeal swabs of symptomatic patients. The **BD Veritor** System for Rapid Detection of Flu A+B (also referred to as the **BD Veritor** System and **BD Veritor** System Flu A+B) is a differentiated test, such that influenza A viral antigens can be distinguished from influenza B viral antigens from a single processed sample using a single device. The test is to be used as an aid in the diagnosis of influenza A and B viral infections. A negative test is presumptive and it is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Negative test results do not preclude influenza viral infection and should not be used as the sole basis for treatment or other patient management decisions. The test is not intended to detect influenza C antigens.

Performance characteristics for influenza A and B were established during January through March of 2011 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the *Morbidity and Mortality Weekly Report* from the CDC entitled "Update: Influenza Activity—United States, 2010-2011 Season, and Composition of the 2011-2012 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses.

If infection with a novel influenza virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to the state or local health department for testing. Virus culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

SUMMARY AND EXPLANATION

Influenza illness classically presents with sudden onset of fever, chills, headache, myalgias, and a non-productive cough. Epidemics of influenza typically occur during winter months with estimated 114,000 hospitalizations[1] and 36,000 deaths[2] per year in the U.S. Influenza viruses can also cause pandemics, during which rates of illness and death from influenza-related complications can increase dramatically.

Patients who present with suspected influenza may benefit from treatment with an antiviral agent especially if given within the first 48 hours of onset of illness. It is important to rapidly distinguish influenza A from influenza B in order to allow physicians a choice in selective antiviral intervention. Moreover, it is important to determine if influenza A or B is causing symptomatic disease in a particular institution (e.g., nursing home) or community, so that appropriate preventative intervention can be taken for susceptible individuals. It is therefore important to not only rapidly determine whether influenza is present, but also which type of influenza virus is present.[3]

Diagnostic tests available for influenza include rapid immunoassay, immunofluorescence assay, polymerase chain reaction (PCR), serology, and viral culture.[4-11] Immunofluorescence assays entail staining of specimens immobilized on microscope slides using fluorescent-labeled antibodies for observation by fluorescence microscopy.[6,12,13] Culture methods employ initial viral isolation in cell culture, followed by hemadsorption inhibition, immunofluorescence, or neutralization assays to confirm the presence of the influenza virus.[13-15]

The **BD Veritor** System for Rapid Detection of Flu A+B is a chromatographic immunoassay to detect influenza A or B nucleoprotein antigens from respiratory specimens of symptomatic patients with a time to result of 10 minutes. The speed and simplified workflow of the **BD Veritor** System for Rapid Detection of Flu A+B makes it applicable as a "STAT" influenza A and B antigen detection test providing relevant information to assist with the diagnosis of influenza.

PRINCIPLES OF THE PROCEDURE

The **BD Veritor** System for Rapid Detection of Flu A+B is a chromatographic assay to qualitatively detect influenza A and B viral antigens in samples processed from respiratory specimens. When specimens are processed and added to the test device, influenza A or B viral antigens bind to anti-influenza antibodies conjugated to detector particles in the A + B test strip. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by the line of antibody on the

membrane. A positive result for influenza A is determined by the **BD Veritor** System Reader when antigen-conjugate is deposited at the Test "A" position and the Control "C" position on the **BD Veritor** System Flu A+B assay device. A positive result for influenza B is determined by the **BD Veritor** System Reader when antigen-conjugate is deposited at the Test "B" position and the Control "C" position in the **BD Veritor** System Flu A+B assay device.

REAGENTS

The following components are included in the **BD Veritor** System for Rapid Detection of Flu A+B kit:

BD Veritor System Flu A+B Devices	30 devices	Foil pouched device containing one reactive strip. Each strip has two test lines of monoclonal antibody specific to either Flu A or Flu B influenza viral antigen and murine monoclonal control line antibodies.
RV Reagent D	30 tubes with 400 µL reagent	Detergent with < 0.1% sodium azide
Flexible minitip flocked swab	30 each	Swab for nasopharyngeal or nasal collection
Control A+/B- Swab	1 each	Flu A Positive and Flu B Negative Control Swab, influenza A antigen (inactive recombinant nucleoprotein) with < 0.1% sodium azide
Control B+/A- Swab	1 each	Flu A Negative and Flu B Positive Control Swab, influenza B antigen (inactive recombinant nucleoprotein) with < 0.1% sodium azide

Materials Required But Not Provided: BD Veritor System Reader (Cat. No. 256055)**,** Timer, Tube Rack for specimen testing

Warnings and Precautions:

1. For *in vitro* Diagnostic Use.
2. Test results are not meant to be visually determined. **All test results must be determined using the BD Veritor System Reader.**
3. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to the state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.
4. Pathogenic microorganisms, including hepatitis viruses, Human Immunodeficiency Virus and novel influenza viruses, may be present in clinical specimens. "Standard Precautions"[16-19] and institutional guidelines should be followed in handling, storing and disposing of all specimens and all items contaminated with blood and other body fluids.
5. Dispose of used **BD Veritor** System test devices as biohazardous waste in accordance with federal, state and local requirements.
6. Reagents contain sodium azide, which is harmful if inhaled, swallowed or exposed to skin. Contact with acids produces very toxic gas. If there is contact with skin, wash immediately with plenty of water. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up.
7. Use the flocked swabs provided with the kit for specimen collection.
8. Other than the flocked swabs that are used for specimen collection, kit components should not make contact with the patient.
9. Do not use kit components beyond the expiration date.
10. Do not reuse the device.
11. Do not use the kit if the Control A+/B- swab and Control B+/A- swab do not yield appropriate results.
12. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
13. To avoid erroneous results, swab specimens must be processed as indicated in the assay procedure section.
14. Specific training or guidance is recommended if operators are not experienced with specimen collection and handling procedures.
15. FluMist® is made from attenuated live flu virus and although the concentration tested (1%) was non-interfering, it is possible when tested with higher concentrations that an influenza A and/or influenza B false positive may occur.

Storage and Handling: Kits may be stored at 2–30°C. DO NOT FREEZE. Reagents and devices must be at room temperature (15–25°C) when used for testing.

SPECIMEN COLLECTION

Acceptable specimens for testing with the **BD Veritor** System Flu A+B test include nasal swabs and nasopharyngeal (NP) swabs. Freshly collected specimens should be processed within 1 hour. It is essential that correct specimen collection and preparation methods be followed. Specimens obtained early in the course of the illness will contain the highest viral titers.

Inadequate specimen collection, improper specimen handling and/or transport may yield a false negative result; therefore, specimen collection requires specific training and guidance due to the importance of specimen quality to accurate test results.

Proper Nasal Swab Sample Collection

1. The **BD Veritor** System Kit includes swabs with a flocked nylon tip for nasal specimen collection.

2. Insert the swab into one nostril of the patient.

3. Rotate the swab two complete 360-degree turns; pressing firmly against the nasal mucosa to help ensure the swab obtains both cells and mucus.

4. Withdraw the swab from the nasal cavity. The sample is now ready for processing using the **BD Veritor** System Kit.

Proper Nasopharyngeal Swab Sample Collection

1. The **BD Veritor** System Kit includes swabs with a flocked nylon tip for nasopharyngeal specimen collection.

2. Insert the swab into one nostril of the patient, reaching the surface of the posterior nasopharynx.

3. Rotate the swab over the surface of the posterior nasopharynx.

4. Withdraw the swab from the nasal cavity. The sample is now ready for processing using the **BD Veritor** System Kit.

Dos and Don'ts of Sample Collection

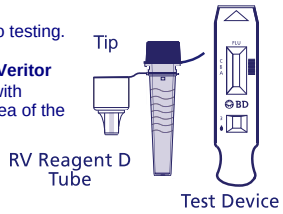
- Do collect sample as soon as possible after onset of symptoms
- Do test sample immediately
- BD recommends flocked swabs which are provided in the **BD Veritor** System Flu A+B Kit
- Do not use cotton tips and wood shafts
- Do not use calcium alginate swabs

PROCEDURES

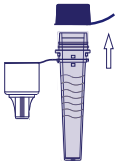
Nasal and Nasopharyngeal Swab Test Procedure

NOTE: Reagents, specimens and devices must be at room temperature (15–25°C) prior to testing.

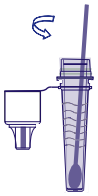
1. For each patient specimen, remove one **RV Reagent D** tube/tip and one **BD Veritor** System Flu A+B device from its foil pouch immediately before testing. Label with patient's name. Place the labeled **RV Reagent D** tube(s) in the designated area of the tube rack.



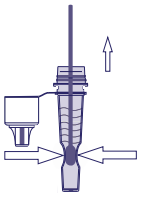
2. Remove and discard the cap from the **RV Reagent D** tube corresponding to the sample to be tested.



3. Insert the patient sample swab all the way into the **RV Reagent D** tube and swirl it against the inside wall three (3) times.

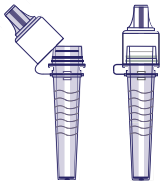


4. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab. Properly discard the swab.

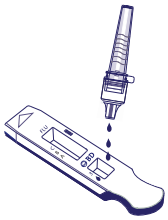


5. Press the attached tip firmly onto the **RV Reagent D** tube containing the processed sample (threading/twisting not required).

   Note: Do not use tips from any other product, including other products from BD or other manufacturers.



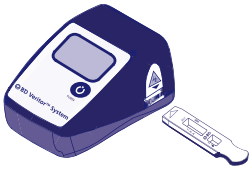
6. Invert the **RV Reagent D** tube and, holding the tube vertically (approximately one inch above the **BD Veritor** System Flu A+B device sample well), squeeze gently on the half of the tube away from the tip, allowing three (3) drops of the processed sample to be dispensed into the sample well of the appropriately labeled **BD Veritor** System Flu A+B device.



7. After adding the sample, allow the test to run for 10 minutes.

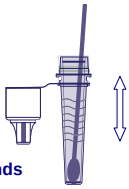
8. When the test is ready, insert the **BD Veritor** System Flu A+B device into the **BD Veritor** System Reader. (The **BD Veritor** System Reader should be powered-on prior to use and will indicate when it is ready for insertion of the **BD Veritor** System device.)

   Follow the reader on-screen prompts to complete the procedure and obtain the test result.



Control Swab Test Procedure

1. Insert the swab all the way into the appropriately labeled **RV Reagent D** tube and vigorously plunge the swab up and down in the fluid for a minimum of 15 seconds.
2. Continue processing the swab according to the Nasal and Nasopharyngeal Test Procedure above beginning at Step 4.



15 seconds

Quality Control:
Each **BD Veritor** System Flu A+B device contains both positive and negative internal/procedural controls:

1. The internal positive control validates the immunological integrity of the device, proper reagent function, and assures that the correct test procedure was followed.
2. The membrane area surrounding test lines functions as a background check on the assay device.

These positive and negative internal/procedural controls are evaluated by the **BD Veritor** System Reader after insertion of the **BD Veritor** System test device. The **BD Veritor** System Reader will prompt the operator should a quality issue occur. Failure of the internal/procedural controls will generate an invalid test result.

External Positive and Negative Controls:
Swab controls (Flu A positive /B negative and Flu B positive/A negative) are supplied with each kit. These controls provide additional quality control material to demonstrate positive or negative assay results using the **BD Veritor** System Reader and **BD Veritor** System test device. BD recommends that positive and negative controls be run once for:

- each new kit lot
- each new operator
- each new shipment of test kits
- as required by internal quality control procedures and in accordance with local, state and federal regulations or accreditation requirements.

If the kit controls do not perform as expected, do not test patient specimens. Contact BD Technical Services at 1-800-638-8663.

INTERPRETATION OF RESULTS

The **BD Veritor** System Reader (purchased separately) must be used for all interpretation of test results. Operators should not attempt to interpret assay results directly from the test strip contained within the **BD Veritor** System Flu A+B assay device.

Reader Display	Interpretation
FLU A: + FLU B: -	Positive Test for Flu A (influenza A antigen present)
FLU A: - FLU B: +	Positive Test for Flu B (influenza B antigen present)
FLU A: - FLU B: -	Negative Test for Flu A and Flu B (no antigen detected)
RESULT INVALID	Result Invalid
CONTROL INVALID	Control line error

Invalid Test – If the test is invalid, the **BD Veritor** System Reader will display a "RESULT INVALID" or "CONTROL INVALID" result and the test or control must then be repeated.

REPORTING OF RESULTS

Positive Test Positive for the presence of influenza A or influenza B antigen. A positive result may occur in the absence of viable virus.

Negative Test Negative for the presence of influenza A or influenza B antigen. Infection due to influenza cannot be ruled-out because the antigen present in the sample may be below the detection limit of the test. It is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay.

Invalid Test Test result is inconclusive. Do not report results. Repeat the test.

LIMITATIONS OF THE PROCEDURE

- Failure to follow the Test Procedure may adversely affect test performance and/or invalidate the test result.
- The contents of this kit are to be used for the qualitative detection of influenza type A and B antigens from nasal swab and nasopharyngeal swab specimens.
- The **BD Veritor** System for Rapid Detection of Flu A+B is capable of detecting both viable and non-viable influenza particles. The **BD Veritor** System for Rapid Detection of Flu A+B performance depends on antigen load and may not correlate with other diagnostic methods performed on the same specimen.
- Results from the **BD Veritor** System for Rapid Detection of Flu A+B test should be correlated with the clinical history, epidemiological data and other data available to the clinician evaluating the patient.
- A false-negative test result may occur if the level of viral antigen in a sample is below the detection limit of the test or if the sample was collected or transported improperly; therefore, a negative test result does not eliminate the possibility of influenza A or influenza B infection, and should be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay.
- Positive test results do not rule out co-infections with other pathogens.
- Positive test results do not identify specific influenza A virus subtypes.
- Negative test results are not intended to rule in other non-influenza viral or bacterial infections.
- Children tend to shed virus for longer periods of time than adults, which may result in differences in sensitivity between adults and children.
- Positive and negative predictive values are highly dependent on prevalence rates. Positive test results are more likely to represent false positive results during periods of little/no influenza activity when disease prevalence is low. False negative test results are more likely during peak influenza activity when prevalence of disease is high.
- This device has been evaluated for use with human specimen material only.
- Monoclonal antibodies may fail to detect, or detect with less sensitivity, influenza A viruses that have undergone minor amino acid changes in the target epitope region.
- The analytical reactivity of this device has not been established for avian or swine origin influenza strains other than those included in the "strain reactivity" tables.
- The performance characteristics of this test with specimens from humans infected with H5N1 or other avian influenza viruses are unknown.
- The performance of this test has not been evaluated for use in patients without signs and symptoms of respiratory infection.

EXPECTED VALUES

The rate of positivity observed in respiratory testing will vary depending on the method of specimen collection, handling/transport system employed, detection method utilized, the time of year, age of the patient, geographic location and most importantly, local disease prevalence. The overall prevalence observed with an FDA-cleared Influenza A and B molecular assay in the U.S. during the 2010-2011 clinical study was 29.9% for Influenza A and 19.7% for influenza B. The overall prevalence observed with the same FDA-cleared Influenza A and B molecular assay in Japan during the 2010-2011 clinical study was 32.2% for Influenza A and 31.7% for influenza B.

PERFORMANCE CHARACTERISTICS

Clinical Performance:

Performance characteristics for the **BD Veritor** System for Rapid Detection of Flu A+B test were established in multi-center Point-of-Care (POC) studies conducted at five U.S. trial sites and eight Japan trial sites during the 2010-2011 respiratory season. A total of 736 prospective specimens (515 in the U.S and 221 in Japan) were tested using the **BD Veritor** System for Rapid Detection of Flu A+B test. These specimens consisted of nasal and nasopharyngeal swabs from symptomatic patients. In the U.S., 54% of the samples were from females and 46% from males. 20.3% of the samples were from patients less than or equal to 5 years of age, 40.8% were from patients in the 6-21 year age group, 35.6% were from 22-59 years of age, and the remaining 3.3% were obtained from people greater than or equal to age 60. In Japan, 43.3% of the samples were from females and 56.7% from males. 27.3% of the samples were from patients less than or equal to 5 years of age, 58.4% were from patients in the 16-21 year age group, 13.1% from 22-59 years of age, and 1.3% were obtained from people greater than or equal to age 60.

The performance of the **BD Veritor** System for Rapid Detection of Flu A+B test at the U.S. sites were compared to an FDA-cleared Influenza A and B molecular assay (PCR).

Explanation of Terms:

PPA: Positive Percent Agreement = a + (a+c) × 100%

NPA: Negative Percent Agreement = d + (b+d) × 100%

P: Positive

N: Negative

C.I.: Confidence Interval

	Comparator Method	
New Test Method	P	N
P	a	b
N	c	d
Total	(a+c)	(b+d)

The performance is presented in Table 1 through Table 3 below.

Table 1: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for All Swabs - U.S. Sites

	Reference PCR		
POC: BD Flu A	P	N	Total
P	122	8	130
N	33*	352	385
Total	155	360	515
Reference Method: PCR PPA: 78.7% (95% C.I. 71.6%-84.4%) NPA: 97.8% (95% C.I. 95.7%-98.9%)			

	Reference PCR		
POC: BD Flu B	P	N	Total
P	75	2	77
N	26**	412	438
Total	101	414	515
Reference Method: PCR PPA: 74.3% (95% C.I. 65%-81.8%) NPA: 99.5% (95% C.I. 98.3%-99.9%)			

* Of the 33 PCR positive, **BD Veritor** negative Influenza A specimens, eight were positive in the **BD Veritor** assay using a second swab specimen (reference method specimen) collected from the same patient.

** Of the 26 PCR positive, **BD Veritor** negative Influenza B specimens, six were positive in the **BD Veritor** assay using a second swab specimen (reference method specimen) collected from the same patient.

Table 2: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for Nasopharyngeal Swabs - U.S. Sites

	Reference PCR		
POC: BD Flu A	P	N	Total
P	53	5	58
N	18	135	153
Total	71	140	211
Reference Method: PCR PPA: 74.6% (95% C.I. 63.4%-83.3%) NPA: 96.4% (95% C.I. 91.9%-98.5%)			

	Reference PCR		
POC: BD Flu B	P	N	Total
P	22	1	23
N	8	180	188
Total	30	181	211
Reference Method: PCR PPA: 73.3% (95% C.I. 55.6%-85.8%) NPA: 99.4% (95% C.I. 96.9%-99.9%)			

Table 3: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for Nasal Swabs – U.S. Sites

	Reference PCR		
POC: BD Flu A	P	N	Total
P	69	3	72
N	15	217	232
Total	84	220	304
Reference Method: PCR PPA: 82.1% (95% C.I. 72.6%-88.9%) NPA: 98.6% (95% C.I. 96.1%-99.5%)			

	Reference PCR		
POC: BD Flu B	P	N	Total
P	53	1	54
N	18	232	250
Total	71	233	304
Reference Method: PCR PPA: 74.6% (95% C.I. 63.4%-83.3%) NPA: 99.6% (95% C.I. 97.6%-99.9%)			

The performance of the **BD Veritor** System for Rapid Detection of Flu A+B test at the Japan sites were also compared to the same FDA-cleared Influenza A and B molecular assay (PCR) and are presented in Table 4 through Table 6.

Table 4: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for all Swabs - Japan Sites

	Reference PCR		
POC: BD Flu A	P	N	Total
P	67	5	72
N	4	145	149
Total	71	150	221
Reference Method: PCR PPA: 94.4% (95% C.I. 86.4%-97.8%) NPA: 96.7% (95% C.I. 92.4%-98.6%)			

	Reference PCR		
POC: BD Flu B	P	N	Total
P	64	8	72
N	6	143	149
Total	70	151	221
Reference Method: PCR PPA: 91.4% (95% C.I. 82.5%-96%) NPA: 94.7% (95% C.I. 89.9%-97.3%)			

Table 5: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for all Nasopharyngeal Swabs - Japan Sites

	Reference PCR		
POC: BD Flu A	P	N	Total
P	30	1	31
N	2	83	85
Total	32	84	116
Reference Method: PCR PPA: 93.8% (95% C.I. 79.9%-98.3%) NPA: 98.8% (95% C.I. 93.6%-99.8%)			

	Reference PCR		
POC: BD Flu B	P	N	Total
P	38	2	40
N	1	75	76
Total	39	77	116
Reference Method: PCR PPA: 97.4% (95% C.I. 86.8%-99.5%) NPA: 97.4% (95% C.I. 91%-99.3%)			

Table 6: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for Nasal Swabs – Japan Sites

	Reference PCR		
POC: BD Flu A	P	N	Total
P	37	4	41
N	2	62	64
Total	39	66	105
Reference Method: PCR PPA: 94.9% (95% C.I. 83.1%-98.6%) NPA: 93.9% (95% C.I. 85.4%-97.6%)			

	Reference PCR		
POC: BD Flu B	P	N	Total
P	26	6	32
N	5	68	73
Total	31	74	105
Reference Method: PCR PPA: 83.9% (95% C.I. 67.4%-92.9%) NPA: 91.9% (95% C.I. 83.4%-96.2%)			

Reproducibility

The reproducibility of the **BD Veritor** System for Rapid Detection of Flu A+B test was evaluated at three POC sites. The reproducibility panel was composed of 30 simulated influenza A or B samples. These included moderate positive samples, low positive samples (near the assay limit of detection), high negative samples (i.e., containing very low concentrations of virus such that positive results occur ~5% of the time) and negative samples. The panel was tested by two operators at each site for five consecutive days. The results are summarized below.

Reproducibility Results – Percent of Flu A Positives				
Sample	**Site 1**	**Site 2**	**Site 3**	**Total**
High negative H1N1 A	0% (0/30) (95% C.I. 0%-11.3%)	10% (3/30) (95% C.I. 3.5%-25.6%)	26.7% (8/30) (95% C.I. 14.2%-44.4%)	12.2% (11/90) (95% C.I. 7%-20.6%)
Low positive H1N1 A	86.7% (26/30) (95% C.I. 70.3%-94.7%)	96.7% (29/30) (95% C.I. 83.3%-99.4%)	100% (30/30) (95% C.I. 88.6%-100%)	94.4% (85/90) (95% C.I. 87.6%-97.6%)
Moderate positive H1N1 A	100% (30/30) (95% C.I. 88.6%-100%)	100% (30/30) (95% C.I. 88.6%-100%)	100% (30/30) (95% C.I. 88.6%-100%)	100% (90/90) (95% C.I. 95.9%-100%)
High negative H3N2 A	0% (0/30) (95% C.I. 0%-11.3%)	10% (3/30) (95% C.I. 3.5%-25.6%)	16.7% (5/30) (95% C.I. 7.3%-33.6%)	8.9% (8/90) (95% C.I. 4.6%-16.6%)
Low positive H3N2 A	100% (30/30) (95% C.I. 88.6%-100%)	93.3% (28/30) (95% C.I. 78.7%-98.2%)	96.7% (29/30) (95% C.I. 83.3%-99.4%)	96.7% (87/90) (95% C.I. 90.7%-98.9%)
Moderate positive H3N2 A	100% (30/30) (95% C.I. 88.6%-100%)	100% (30/30) (95% C.I. 88.6%-100%)	100% (30/30) (95% C.I. 88.6%-100%)	100% (90/90) (95% C.I. 95.9%-100%)
Negatives	0% (0/119) (95% C.I. 0%-3.1%)	0.8% (1/119) (95% C.I. 0.1%-4.6%)	0% (0/119) (95% C.I. 0%-3.1%)	0.3% (1/357) (95% C.I. 0%-1.6%)

Reproducibility Results – Percent of Flu B Positives				
Sample	**Site 1**	**Site 2**	**Site 3**	**Total**
High negative B	0% (0/30) (95% C.I. 0%-11.3%)	3.3% (1/30) (95% C.I. 0.6%-16.7%)	26.7% (8/30) (95% C.I. 14.2%-44.4%)	10% (9/90) (95% C.I. 5.4%-17.9%)
Low positive B	73.3% (22/30) (95% C.I. 55.6%-85.8%)	90% (27/30) (95% C.I. 74.4%-96.5%)	90% (27/30) (95% C.I. 74.4%-96.5%)	84.4% (76/90) (95% C.I. 75.6%-90.5%)
Moderate positive B	100% (29/29) (95% C.I. 88.3%-100%)	96.6% (28/29) (95% C.I. 82.8%-99.4%)	100% (29/29) (95% C.I. 88.3%-100%)	98.9% (86/87) (95% C.I. 93.8%-99.8%)
Negatives	0% (0/210) (95% C.I. 0%-1.8%)	1.0% (2/210) (95% C.I. 0.3%-3.4%)	0% (0/210) (95% C.I. 0%-1.8%)	0.3% (2/630) (95% C.I. 0.1%-1.2%)

Analytical Studies

Analytical Sensitivity (Limit of Detection)

The limit of detection (LOD) for the **BD Veritor** System for Rapid Detection of Flu A+B test was established for a total of 7 influenza strains: 4 influenza A and 3 influenza B. The LOD for each strain represents the lowest concentration producing a positivity rate of ≥95% based on testing 20 to 60 replicates.

Type	Influenza Viral Strain	Calculated LOD ($TCID_{50}$/mL)	No. Positive / Total	% Positive
A	A/Brisbane/10/2007 H3N2	7.27×10^{2}	57/60	95%
A	A/Brisbane/59/2007 H1N1	3.30×10^{2}	57/60	95%
A	A/California/7/2009 H1N1	5.00×10^{3}	57/60	95%
A	A/Victoria/3/75 H3N2	3.11×10^{3}	59/60	98.3%
B	B/Brisbane/60/2008	7.42×10^{3}	58/60	96.7%
B	B/Florida/4/2006	1.30×10^{3}	58/60	96.7%
B	B/Lee/40	4.44×10^{4}	20/20	100%

$TCID_{50}$/mL = 50% Tissue Culture Infectious Dose

Strain Reactivity with Influenza A and B Viruses

The **BD Veritor** System for Rapid Detection of Flu A+B test was evaluated using a panel of 52 influenza strains. All influenza A strains showed positive Flu A test results and negative Flu B test results. Conversely, all of the influenza B strains showed positive Flu B test results and negative Flu A test results.

Influenza A Viral Strains
A/Aich2/68
A/Brisbane/10/2007
A/Brisbane/59/2007
A/California/7/2009
A/Denver/1/57
A/FM/1/47
A/Hong Kong/8/68
A/New Caledonia/20/1999
A/New Jersey/8/76
A/NWS/33
A/Perth/16/2009
A/Port Chalmers/1/73
A/PR/8/34
A/Wisconsin/67/2005
A/Victoria/3/75
A/Weiss/43
A/Mal/302/54
A/WS/33
A/Moscow/10/99
A/Solomon Island/03/2006

Influenza B Viral Strains
B/Brazil/178/96
B/Brisbane/60/2008
B/Brisbane/72/97
B/Canada/548/99
B/Egypt/00393/99
B/Florida/2/2006
B/Florida/4/2006
B/Fujian/93/97
B/Fukushima/220/99
B/GuangXi/547/98
B/Hawaii/01/97
B/Hong Kong/5/72
B/Hong Kong/219/98
B/Jiangsu/10/2003
B/Johannesburg/5/99
B/Lee/40
B/Lisbon/03/96
B/Malaysia/2506/2004
B/Maryland/1/59
B/Mass/3/66
B/Ohio/1/05
B/Ohio/11/96
B/Puerto Mont/10427/98
B/Russia/69
B/Shangdong/7/97
B/Shanghai/04/97
B/Shenzhen/135/97
B/Sichuan/116/96
B/Taiwan/2/62
B/Victoria/504/00
B/Yamanashi/166/98
B/Yamagata/16/88

Analytical Specificity (Cross Reactivity)

The **BD Veritor** System for Rapid Detection of Flu A+B test was evaluated with a total of 51 microorganisms. The 37 bacteria and yeast were tested at a target concentration of approximately 10^7 CFU/mL (CFU – Colony Forming Units) with the exception of *Staphylococcus aureus,* which was tested at a final concentration of 10^6 CFU/mL. The 14 viruses were evaluated at concentrations of 10^3 to 10^{10} $TCID_{50}$/mL. Of the 51 microorganisms tested, none showed cross-reactivity in either the Flu A or Flu B tests.

Bacteriodes fragilis
Bordetella pertussis
Candida albicans
Chlamydia pneumoniae
Corynebacterium diphtherium
Escherichia coli
Fusobacterium nucleatum
Haemophilus influenzae
Haemophilus parainfluenzae
Kingella kingae
Klebsiella pneumoniae
Lactobacillus sp.
Legionella sp.
Moraxella catarrhalis
Mycobacterium tuberculosis
Mycoplasma pneumoniae
Neisseria gonorrhoeae
Neisseria meningitidis
Neisseria mucosa
Neisseria sp.*(Neisseria perflaus)*
Neisseria subflava
Peptostreptococcus anaerobius
Porphyromonas asaccharolyticus
Prevotella oralis
Propionibacterium acnes
Proteus mirabilis
Pseudomonas aeruginosa
Serratia marcescens
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus sp. Group C
Streptococcus sp. Group G
Streptococcus salivarius
Veillonella parvula

Adenovirus, type 1
Adenovirus, type 7
Cytomegalovirus
Enterovirus
Epstein Barr Virus
HSV Type 1
Human Coronavirus OC43
Human Coronavirus 2229E
Human metapneumovirus (HMPV-27 A2)
Human Parainfluenza
Measles virus
Mumps virus
Respiratory syncytial virus
Rhinovirus

Interfering Substances

Various substances were evaluated with the **BD Veritor** System for Rapid Detection of Flu A+B test. These substances included whole blood (2%) and various medications. No interference was noted with this assay for any of the substances tested.

Substance	Concentration
Whole Blood	2%
4-Acetamidophenol	10 mg/mL
Acetylsalicylic acid	20 mg/mL
Chlorpheniramine maleate	5 mg/mL
Dextromethorphan	10 mg/mL
Diphenhydramine HCl	5 mg/mL
Guaiacol Glyceryl Ether	20 mg/mL
Ibuprofen	10 mg/mL
Loratidine	100 ng/mL
Menthol Throat Lozenges	10 mg/mL
Ayr Saline Nasal Gel	10 mg/mL
Oxymetazoline	0.05 mg/mL
Phenylephrine	1 mg/mL
Pseudoephedrine HCl	20 mg/mL
Three OTC mouthwashes	5 %
Four OTC nasal sprays	10 %
Four OTC throat drops	25 %
Homeopathic Allergy Medicine	10 mg/mL
Albuterol	0.083 mg/mL
Amantadine Hydrochloride	500 ng/mL
Beclomethasone	500 ng/mL
Budesonide	500 ng/mL
Dexamethasone	10 mg/mL
Fexofenadine	500 ng/mL
FluMist	1%
Flunisolide	500 ng/mL
Fluticasone	500 ng/mL
Mometasone	500 ng/mL
Mupirocin	500 ng/mL
Oseltamivir	500 ng/mL
Purified Mucin Protein	1 mg/mL
Ribavirin	500 ng/mL
Rimantadine	500 ng/mL
Tobramycin	500 ng/mL
Triamcinolone	500 ng/mL
Zanamivir	1 mg/mL

Of the 43 substances tested in this study, none exhibited interfering reactions when tested with influenza A and influenza B positive samples. Based on the data, the substances tested at the indicated concentration levels did not interfere with the **BD Veritor** System for Rapid Detection of Flu A+B test.

CLIA WAIVER STUDY

As part of a larger prospective study, as described in the Performance Characteristics section above, the accuracy of the **BD Veritor** System for Rapid Detection of Flu A+B test was evaluated at five CLIA waived testing sites. A total of 31 operators representative of CLIA waived sites (intended users) participated in the study. No training on the use of the test was provided. The study included 515 nasal/nasopharyngeal swabs prospectively collected and 80 retrospective archived specimens. The **BD Veritor** System results were compared with results obtained by an FDA cleared molecular influenza A and B assay, the comparator method. Three specimens were excluded due to **BD Veritor** invalid results. The invalid rate was 0.5% (3/598) with 95% CI: 0.2% to 1.5%.

The positive percent agreement (PPA) and the negative percent agreement (NPA) between the **BD Veritor** results and the comparator method are presented in the tables below (refer to Performance Characteristics section for definition of terms).

INFLUENZA A				
Positive Percent Agreement and Negative Percent Agreement of BD Veritor Flu A+B Test with the Comparator Method				
Total Number of Samples	**PPA**	**95% Exact Confidence Interval**	**NPA**	**95% Exact Confidence Interval**
595	82.1% (151/184)	(75.9%, 86.9%)	98.1% (401/411)	(96.2%, 99.0%)

INFLUENZA B				
Positive Percent Agreement and Negative Percent Agreement of BD Veritor Flu A+B Test with the Comparator Method				
Total Number of Samples	**PPA**	**95% Exact Confidence Interval**	**NPA**	**95% Exact Confidence Interval**
595	79.7% (102/128)	(71.9%, 85.7%)	99.4% (464/467)	(98.1%, 99.8%)

Another study was designed to assess the capability of untrained users to test weakly reactive samples and deliver results with accuracy. The **BD Veritor** System for Rapid Detection of Flu A+B assay was evaluated at three non-laboratory CLIA waived sites using panels of simulated swab samples including two weak positives near the assay cutoff and one negative sample. The positive swab samples were formulated at two levels: a "low positive" sample targeted at the assay limit of detection; and a "high negative" sample targeted just below the assay limit of detection. The panels included two strains of Flu A viruses (A/California/7/2009 and A/Victoria 3/75) and one Flu B virus (B/Lee/40). The swab samples were randomized and masked with respect to their identity. There were two intended users at each of the CLIA waived sites (six operators in total) and each site tested the panel on each of 10 days. The same panels of simulated swab samples were also tested at three clinical laboratory sites as controls. The performance of the **BD Veritor** System with samples near the assay cutoff was acceptable when used by intended users.

The tables below show performance of the test with samples near the cutoff of the assay for influenza A and influenza B in the hands of untrained intended users (across all sites).

Influenza A Viral Strains		
	Untrained Intended Users	
Sample Type	**Percent Detection**	**95% Confidence Interval**
High Negative A/California/7/2009 H1N1	6.7% (4/60)	2.6%, 15.9%
Low Positive A/California/7/2009 H1N1	81.7% (49/60)	70.1%,89.4%
High Negative A/Victoria 3/75 H3N2	6.7% (4/60)	2.6%, 15.9%
Low Positive A/Victoria 3/75 H3N2	80.0% (48/60)	68.2%, 88.2%
Negative	0% (0/118)*	0%, 3.2%

*Two (2) samples were excluded from the analysis due to errors in data recording.

Influenza B Viral Strain		
	Untrained Intended Users	
Sample Type	**Percent Detection**	**95% Confidence Interval**
High Negative B/Lee/40	11.7% (7/60)	5.8%, 22.2%
Low Positive B/Lee/40	72.4% (42/58)*	59.8%, 82.2%
Negative	0% (0/240)	0%, 1.6%

*Two (2) samples were excluded from the analysis due to errors in data recording.

Using risk analysis as a guide, analytical flex studies were conducted. The studies demonstrated that the test is insensitive to stresses of environmental conditions and potential user errors.

In support of the CLIA waiver, an additional reactivity study was performed at an independent laboratory to demonstrate reactivity of the **BD Veritor** System for the Rapid Detection of Flu A+B with a broad range of contemporary influenza A and influenza B viruses. The **BD Veritor** System yielded positive results with all 18 influenza A viruses and 7 influenza B viruses included in the test panel at acceptable viral load levels.

AVAILABILITY

Cat. No.	**Description**
256045	**BD Veritor™** System for Rapid Detection of Flu A+B, 30 tests
256055	**BD Veritor™** System Reader

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